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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

YAO, LEI

ART UNIT

PAPER NUMBER

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/014,887	Applicant(s) KRISSENSSEN ET AL.	
	Examiner LEI YAO	Art Unit 1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on 29 March 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3, 10, 11, 13-15, 18, 19, 21-23, 26, 27, 29-31 and 56-58 is/are pending in the application.
- 4a) Of the above claim(s) 10, 11, 15, 18, 19, 23, 26, 27 and 31 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3, 13, 14, 21, 22, 29, 30 and 56-58 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>5/26/2009</u> . | 6) <input type="checkbox"/> Other: _____ |

Response to Amendment and Arguments

The Amendment filed on 3/23/2009 in response to the previous Non-Final Office Action (12/22/2009) is acknowledged and has been entered.

Claims 4-9, 12, 16-17, 20, 24-25, 28, 32-55 are cancelled.

Claims 1-3, 10-11, 13-15, 18-19, 21-23, 26-27, 29-31, 56-58 are pending.

Claims 10-11, 15, 18-19, 23, 26-27, and 31 were previously withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention,

Claims 1-3, 13-14, 21-22, 29-30, and 56-58, drawn to a method of treating for a mammal or a patient with a cancer by administering DMXAA and a DNA encoding B7.1, are currently under examination.

Information Disclosure Statement

The information disclosure statement (s) (IDS) submitted on 5/26/2009 are/is considered by the examiner and initialed copies/copy of the PTO-1449 are/is enclosed.

Rejection Maintained and Response to Arguments

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

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(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148

USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Amended claims 1-3, 13-14, 21-22, 29-30, and 56-58 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Emtage et al., (J Immuno. Vol 160, page 2531-38, 1998) in view of Wilson et al., (Int. J. Radiation Oncology Biol. Phys., Vol. 42, page 905-908, 1998, provided 10/9/2007) or Lash et al., (Br. J Cancer. Vol 78, page 439-45, 1998, abstract).

The Office acknowledges that claims 1-2 are amended to delete the specific dose of DNA administration in the claimed method. However, the claims are still drawn to the same method of treating tumor with B7.1 DNA (no dose limitation) in combination of DMXAA, which would still be unpatentable over the combination of the references for the reasons below.

Applicant argues that neither of Emtage et al., Wilson et al or Lash et al teach administering DNA encoding B7.1 in any amount prior to administering an optimal dose of DMXAA and the cited references do not teach the specific order of administration

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(page 7). In response, claimed method is combination therapy with two or more reagents. It has been clear for one skilled in the art that B7.1 DNA requires a period of time to be expressed and then to stimulate the host immune response against tumor, whereas reagent DMXAA is a chemical, it would be obvious to one skilled in the art to give the B7.1 DNA prior to DMXAA in order to let the two reagents acting at same time.

Applicant then argues that there is no suggestion or motivation in the cited references, specifically the references teach the combinational therapy with the reagents having different actions. In response, combinational therapy with two or more known anti-cancer drugs acting in differently is routinely used and would be obvious and ready to be combined in the cancer field because the skilled artisans understand that many factors in the host system are required or involved in a cancer development and therefor used for the cancer treatment. Thus, one skilled in the art are currently motivated with reasonable expectation to be successful to use two or more anti-cancer agent together for treating their patients because each one acts differently and would have an additive result. Using two or more already known anti-cancer reagents together for treating a cancer is not patentable over the references teaching them for individual treatment unless unexpected result are observed in such combination. The Office considers that references provided in the rejection is even stronger than the argument above, since Emtage et al teach B7.1 DNA in combination with cytokine, a T-cell growth factor, IL-2 activating T cell to against tumor. Replacing IL-2 with DMXAA is reasonable and the result would be expected because Wilson et al teach that DMXAA induces cytokine TNF that is a potential activator of T-cell through different pathway. In addition,

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the Office also provides a reference of Lash et al who teach that skilled artisan has already treated cancer with DMXAA in combination with another anti-cancer agent. Thus, one of ordinary skill in the art at the time the invention would arrive at the current invention absent unexpected results.

At page 8, Applicant argues that *in the Office Action dated April 28, 2008, the Office cited Olsson et al that apparently teach that human IL-2 is induced by B7.1 and it is obvious to replace the IL-2 with B7.1 with an expected result. According to this Office, IL-2 is replaceable with B7.1. The citation of Emtage et al. (in this action) demonstrates that B7.1 and IL-2 are not replaceable as previously alleged by the Office.* In response, Applicant's argument is considered but not persuasive. First, providing a new and considering as a better reference in the Office action to the RCE filed (10/21/2008) is proper. The Office has clearly stated the motivation and reasonable expectation of success for each of the combinations in those the Office actions. However, in response to the argument above, the Office consider both primary references used in the two different actions are not only reasonable, but, In fact, the two references are well connected and even supported each other. Olsson teaches that IL-2 is induced by B7.1, Emtage et al. teach using both B7.1 and IL-2, thus, Emtage teaches using double amount of IL-2, is it reasonable to replace the IL-2 self and leave the B7.1 with DMXAA, a TNF inducer and potential activator of T-cell for combinational therapy?

Applicant at page 9-10, further argues that there is no reasonable expectation of success and states that meanwhile, the instant specification shows surprising results that combined therapy by timed delivery of B7.1 and DMXAA. In response, first, the

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result of combining any two already known anti-cancer agents for treating a cancer would be expected because these reagents have been known and used for the same cancer treatment. Regarding the surprising results of combined therapy by timely delivery of B7.1 and DMXAA to eradicate large tumor, the Office would require more evidence to support the claimed invention, such as the large tumor could not be treated or eradicated by each of the agents individually and/or the result is unexpected etc. Simply providing the treatment result would not be enough because anti-tumor immunity by activated T-cell is well known and practiced to eradicate an established tumor, not tumor prevention or inhibition of tumor cell growth.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lei Yao, Ph.D. whose telephone number is 571-272-3112. The examiner can normally be reached on 8am-6.00pm Monday-Thursday.

Any inquiry of a general nature, matching or file papers or relating to the status of this application or proceeding should be directed to Kim Downing for Art Unit 1642 whose telephone number is 571-272-0521

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Lei Yao/
Examiner, Art Unit 1642

/Larry R. Helms/

Supervisory Patent Examiner, Art Unit 1643